

Guideline Series 84: MUTAGENICITY

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Toxicology Branch-I (7509C)

DATA EVALUATION REPORT

STUDY TYPE: Salmonella/mammalian activation gene mutation assay

TOX. CHEM. NO.: 253

P.C.CODE: 024002

MRID NUMBER: 429623-01

TEST MATERIAL: Copper 8-Quinolinate

SYNONYMS: Ro 17-0099/000; oxine-copper (copper oxinate)

STUDY NUMBER(S): B-116'875

SPONSOR: (042567) La Quinoleine SA, via U.S. agent: International Regulatory Consulting, Washington, DC

TESTING FACILITY: F. Hoffmann-La Roche, Basel, (Switzerland)

TITLE OF REPORT: Mutagenicity Evaluation of the Fungicide Ro 17-0099/000 (Copper 8-Quinolinate) with Salmonella typhimurium (Ames Test)

AUTHOR(S): A. Ch<sup>é</sup>telat

REPORT ISSUED: July 5, 1989

CONCLUSION(S) - Executive Summary:

Dose-related weakly positive for reverse gene mutation in S9-activated bacterial strains TA97, TA100, TA102 of S. typhimurium exposed up to toxic doses.

Classification: ACCEPTABLE

This study does satisfy the requirement for FIFRA Test Guideline 84-2 for in vitro mutagenicity (bacterial reverse gene mutation) data.

[TECHNICAL NAME] SALMONELLA/MAMMALIAN ACTIVATION; GENE MUTATION

A. MATERIALS

1. Test Material: Ro 17-0099/000  
Description : Olive-green crystalline powder  
Lot/Batch #: 211-188  
Purity: 99.7% a.i.  
Stability of compound: Two years in closed container  
CAS #: 10380-28-6  
Structure: BIS (8-QUINOLINOLATO) COPPER [ $C_{18}H_{12}CuN_2O_2$ ]  
Solvent used: Dimethylsulfoxide  
Other comments: [None]

2. Control Materials:

Solvent/final concentration: 1%

Positive: Non-activation:

Sodium azide, 1  $\mu$ g/plate for TA100, TA1535, TA1537

2-Nitrofluorene, 0.5  $\mu$ g/plate for TA98, TA1538

Other: ICR-191, 1  $\mu$ g/plate for TA97

MMC, 0.4  $\mu$ g/plate for TA102

Activation:

2-Aminoanthracene (2-anthramine) 4.0  $\mu$ g/plate for all strains

~~Other:~~

3. Activation: S9 derived from

<input checked="" type="checkbox"/> Aroclor 1254	<input checked="" type="checkbox"/> induced	<input checked="" type="checkbox"/> rat	<input checked="" type="checkbox"/> liver
<input checked="" type="checkbox"/> phenobarbital/	<input type="checkbox"/> non-induced	<input type="checkbox"/> mouse	<input type="checkbox"/> lung
<input type="checkbox"/> beta-naphthoflavone (rat liver)		<input type="checkbox"/> hamster	<input type="checkbox"/> other
<input type="checkbox"/>		<input type="checkbox"/> other	

Describe S9 mix composition:

S9, 0.1 ml      NADP, 3.2 mg

Kcl, 0.165M      G-6-P, 1.53 mg

mgcl, 0.04M

4. Test organisms: S. typhimurium strains (seven in current use)

☒ TA97 ☒ TA98 ☒ TA100 ☒ TA102 ☐ TA104

☒ TA1535 ☒ TA1537 ☒ TA1538;

Properly maintained? Yes

Checked for appropriate genetic marker: Yes

[TECHNICAL NAME] SALMONELLA/MAMMALIAN ACTIVATION; GENE MUTATION

5. Test compound concentrations used:

Non-activated conditions: 0.33 - 100.0  $\mu\text{g}/\text{plate}$  (standard assay)

0.51 - 50.0  $\mu\text{g}/\text{plate}$  (pre-incubation)

Activated conditions:

0.33 - 100.0  $\mu\text{g}/\text{plate}$  standard assay)

0.51 - 50.0  $\mu\text{g}/\text{plate}$  (preincubation)

B. TEST PERFORMANCE

1. Type of Salmonella assay: ☒ standard plate test  
☒ pre-incubation (30 minutes)  
☐ "Prival" modification  
☐ spot test  
☐ other (describe in a.)

2. Protocol: According to Ames (1975), Maron and Ames (1983), inter alia

C. REPORTED RESULTS

1. Preliminary cytotoxicity assay: Strain TA100 exposed to six concentrations, 0.32 through 1000  $\mu\text{g}/\text{plate}$ ; precipitation and cytotoxicity at 200 and 1000  $\mu\text{g}/\text{plate}$ .
2. Mutagenicity assay: In standard plate assays, no increase in revertants in TA 1538 ( $\pm\text{S9}$ ), TA98 ( $\pm\text{S9}$ ), TA100 ( $-\text{S9}$ ), TA1535 ( $\pm\text{S9}$ ), TA1537 ( $\pm\text{S9}$ ) up to cytotoxic doses (33, 100  $\mu\text{g}/\text{plate}$ ), but slight increases (1.2 X background) in S9-activated TA97, TA100 and TA102. In pre-incubation series, no increase up to cytotoxicity in any non-activated cultures, but dose-dependent increased reversions noted for activated TA97, TA100 and TA102 (all less than 2X background). Hence the investigator concluded that the test article was weakly mutagenic in some activated Salmonella strains at mild to moderate toxic concentrations.

- D. REVIEWER'S DISCUSSION/CONCLUSIONS: ACCEPTABLE. No major deficiencies in this minimally positive study.

- E. Was test performed under GLPs (is a quality assurance statement present)? Yes.

- F. Appendix attached: Yes, Data Tables.

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[TECHNICAL NAME] SALMONELLA/MAMMALIAN ACTIVATION; GENE MUTATION

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DER. MRID# 429623-01 Copper 8-Quinolinolate

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